forth earlier in the Office Action, i.e. on pages 2-8, were being maintained, along with the new rejection set forth beginning on page 10.

The Examiner also confirmed that the reference to the Amendment of July 9, 2008 in the second paragraph on page 2 of the Office Action should have referred to the Amendment of June 25, 2008. [Apparently this same correction should be made in the first line under the "Response to Arguments" section on page 8 of the Office Action, i.e. the Examiner meant to refer to Applicant's arguments filed June 25, 2008, instead of July 7, 2008.]

Patentability Arguments

The rejection of claims 1-11 under 35 U.S.C. §103(a) as being unpatentable over Harris et al. (US '450) in view of Daniel et al. (WO '560), set forth beginning on page 2 of the Office Action, is respectfully traversed.

At page 3, lines 4-6 of the Office Action, the Examiner states that Harris et al. do not specifically teach or make provision that the formulation "does not contain a substantial amount of a saccharide compound." Although this language, that the formulation does not contain a substantial amount of a saccharide compound, was earlier included in claim 1 (the only independent claim under consideration), it was deleted by the Amendment filed April 25, 2008. A copy of the pending claims, including amended claim 1 was attached to the Advisory Action mailed May 21, 2008, with the notation that the amendment to claim 1 will not be entered. Applicant then filed an RCE on June 25, 2008, requesting that the Amendment filed April 25, 2008 be entered. Accordingly, the claims presently pending in the application are those set forth in the Amendment filed April 25, 2008. **As noted above, the previous language that the formulation "does not contain a substantial amount of a saccharide compound" has been deleted; and language specifying that the formulation contain "less than 5 wt% of a saccharide compound" was added to claim 1.**

In this regard, referring to the first full paragraph on page 8 of the current Office Action, the Examiner states that "The prior art teaches away from a formulation of an ACE inhibitor composition that contains less than 5 wt% (formerly claim 14, which has been incorporated into

claim 1) or less than 2 wt% (claim 15) of a saccharide compound." The Examiner states that claims 14-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base and any intervening claims. **Since claim 1 has already been amended to incorporate the subject matter of claim 14, it is apparent that claim 1 (as well as all of the other claims, which are dependent on claim 1) are allowable over Harris et al. in view of Daniel et al.**

This same reasoning applies to the rejection of claims 12-13 and 16 under 35 U.S.C. §103(a) as being unpatentable over Harris et al. in view of Daniel et al., as set forth on page 6 of the Office Action (although Applicant notes that claim 13 was previously cancelled).

Thus, considering the Examiner's statement in the first full paragraph on page 8 of the Office Action, it is apparent that the only rejection remaining for consideration is the rejection of claims 1-12 and 15-16 under 35 U.S.C. §103(a) as being unpatentable over Harris et al. in view of Daniel et al. in further view of de Haan et al. (US '520), which is respectfully traversed.

Harris et al. teach that at least 5% saccharide is necessary in their ACE inhibitor formulation. They also disclose, in Example D, an inoperative formulation without any saccharide.

Daniel et al. teach an ACE inhibitor formulation which contains a stabilizer (magnesium oxide) and 10-95% hydrolysis-minimizing agent (including saccharides and dicalcium phosphate). Saccharides are most preferred.

The Examiner asserts that it would have been obvious for a skilled person to include an insoluble alkaline-earth metal salt of hydrogen phosphate (dicalcium hydrogen phosphate) in the composition of Harris et al. to replace the saccharide (which the Examiner asserts are taught as functional equivalents by Daniel et al.).

The Examiner asserts that de Haan et al. provide the motivation to exclude a saccharide in the composition, as de Haan et al. point out that Harris et al. specifically require a saccharide component in the described composition, which unnecessarily increases production costs (column 2, lines 34-37 of de Haan et al.).

Briefly, de Haan et al. disclose a dry chemical composition containing "the water soluble acid addition salt of a poorly soluble basic compound" (e.g. mianserin, apomorphine, chlopromazine, imipramine or promethazine), an excipient including calcium hydrogen phosphate, and a water soluble alkaline stabilizer. This composition is said to be more stable than a formulation not containing a water-soluble alkaline stabilizer.

However, de Haan et al. do not suggest any saccharide-free **ACE inhibitor** formulation. If the Examiner insists that de Haan et al.'s invention applies to an ACE-inhibitor, she must show that one of ordinary skill in the art would have a reasonable expectation of success in achieving a stabilized saccharide-free ACE inhibitor formulation by combining the references in the manner suggested by the Examiner (MPEP 2143.02).

The Examiner specifically refers to Example 1 of de Haan et al. (saccharide-free formulation) which contains **mianserin HCl**, $NaHCO_3$ (alkali metal carbonate), and calcium hydrogen phosphate (insoluble alkaline-earth metal salt of hydrogen phosphate). This particular composition is totally unrelated to an ACE-inhibitor. As suggested in column 3, lines 10-11 and claim 1 of de Haan et al., the active ingredients contemplated are "mianserin, apomorphine, chlorpromazine, imipramine and promethazine." Nowhere do de Haan et al. suggest that an ACE-inhibitor is also applicable. While it is true that de Haan et al. mention Harris et al. in the **background** section (column 2, line 34), this does not imply that mianserin HCl can be replaced by an ACE-inhibitor with a reasonable expectation of success.

Further, de Haan et al. do **not** advocate omission of a saccharide; they in fact specifically include the saccharide **lactose** as a proposed excipient, see column 2, line 67, abstract and claim 1. De Haan et al.'s reference to Harris et al. is rather to highlight the fact that Harris et al. do not include a water-soluble alkaline stabilizer, which is included as an essential part of de Haan et al.'s invention (see de Haan et al., column 3, lines 3-5).

The de Haan et al. reference does mention that Harris et al., by requiring a saccharide, adds to the cost of such compositions. This statement is unsubstantiated, because lactose and other common saccharide excipients are certainly not expensive. [If necessary, Applicant can find supporting documentation for this.]

Summarizing thus far, de Haan et al. cannot be said to teach away from using a saccharide. They fail to provide a saccharide-free **ACE-inhibitor formulation**, and there is no suggestion that the reference teaching is applicable for an ACE-inhibitor.

The Examiner also asserts that Daniel et al. teach that dicalcium phosphate and saccharide are functional equivalents, and that a skilled artisan would therefore add dicalcium phosphate to the inoperative formulation in Example D of Harris et al. to make it operative. This is mere speculation.

Thus, since Daniel et al. already teach that saccharide is particularly preferred (page 9, line 14), it is therefore questionable that saccharide and dicalcium phosphate can be viewed as "equivalent", based on Daniel et al.'s teaching, simply because these compounds are listed in a broad group of agents referred to by Daniel et al. as "hydrolysis-minimizing agents", which further includes such different compounds as diuretics and hydrochlorothiazide. Applicant also emphasizes that Daniel et al. teach the use of these compounds in **combination** with the stabilizer magnesium oxide.

A skilled person, reading Daniel et al. and contemplating avoiding using a saccharide, would not know at all whether dicalcium phosphate itself would make an inoperative formulation (Example D of Harris et al.) operative, because nowhere is it suggested that dicalcium phosphate and saccharide are "equivalent." There is no reasonable expectation of success, and the prior art as a whole still points to more than 5% of saccharide (as acknowledged by the Examiner on page 8 of the Office Action) for stabilizing an ACE inhibitor.

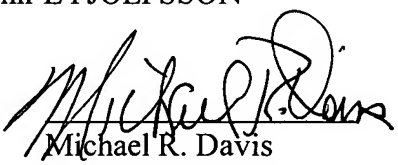
None of the applied references contains all of the limitations of the instantly claimed formulations, and there is no reasonable expectation of success of achieving a stabilized saccharide-free ACE inhibitor formulation by combining the references.

For these reasons, Applicant takes the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Reynir EYJOLFSSON

By: 

Michael R. Davis
Registration No. 25,134
Attorney for Applicant

MRD/pth
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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